

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1 - 35. (Cancelled)

36. (Currently amended) A ~~non-human~~ transgenic mouse ~~mammal~~, ~~comprising an wherein~~ an endogenous IgH locus comprises ~~which is modified by~~ replacement of a its switch sequence S μ with a transgene comprising a human class A immunoglobulin heavy chain constant region gene C α or a segment of said C α gene comprising at least an exon encoding the CH3 domain and a membrane exon, wherein said transgenic mouse produces chimeric immunoglobulins A whose heavy chains comprise a mouse variable region and a human constant region or a segment thereof comprising at least the CH3 domain, and wherein said transgenic mouse produces no immunoglobulins.

37. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 36, which is homozygous for said modified IgH locus.

38. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 36, wherein said endogenous IgH locus ~~is modified by replacement of the switch sequence S μ , with~~ transgene comprises the entire C α gene.

39. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 36, wherein said endogenous IgH locus ~~is modified by replacement of the switch sequence S μ with~~ transgene comprises the segment of the C α gene comprising the exon encoding the CH3 domain and the membrane exon.

40. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 36, wherein said C α gene is the C α 1 gene.

41. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 36, which further comprises another transgene encoding a human immunoglobulin light chain.

42. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 41, wherein said light chain is a kappa light chain.

43. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 41, wherein said ztransgene which encodes a human immunoglobulin kappa light chain, further comprises the intronic activator E μ upstream of a DNA sequence encoding said human immunoglobulin kappa light chain and the palindrome *hs3a/hs1,2/hs3b* downstream of said DNA sequence.

44. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 43, wherein said transgene is under the control of the promoter of the human immunoglobulin heavy chain.

45. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 41, which is dizygous for said transgene.

46. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 41, further comprising an inactivated endogenous immunoglobulin kappa light chain locus.

47. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 46, which is homozygous for said inactivated endogenous immunoglobulin kappa light chain locus.

48. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 36, further comprising an inactivated endogenous J chain gene.

49. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 48, which is homozygous for said inactivated endogenous J chain gene.

50. (Currently Amended) The ~~non-human~~ transgenic ~~mammal~~ mouse of claim 48, which further comprises another transgene encoding a human immunoglobulin J chain gene.

51. (Canceled)

52. (Currently Amended) A The transgenic mouse of claim 36 ~~51~~, ~~which comprises:~~ wherein
said:

a) ~~an~~ endogenous mouse IgH locus comprises the ~~modified by~~ replacement of ~~the~~ its switch sequence $S\mu$ with the entire human class A immunoglobulin heavy chain constant region gene $C\alpha 1$, and

b) which transgenic mouse further comprises a human kappa light chain transgene comprising a $V\kappa I$ gene rearranged with a $J\kappa 5$ gene, a $J\kappa$ - $C\kappa$ intron and a $C\kappa$ gene, under the transcriptional control of the human heavy chain promoter (pVH), the intronic activator $E\mu$ upstream of said promoter of and the palindrome $hs3a/hs1,2/hs3b$ downstream of said $C\kappa$ gene.

53. (Currently Amended) A homologous recombination targeting vector, which comprises a human class A immunoglobulin heavy chain constant region gene $C\alpha$ or a segment of said $C\alpha$ gene comprising at least an exon encoding the CH3 domain and a membrane exon, flanked by fragments of sequences of the mouse IgH locus ~~from a non-human mammal~~ which are adjacent to a its switch sequence $S\mu$.

54. (Previously presented) The targeting vector of claim 53, which comprises a cassette for expressing a selection marker, adjacent to said $C\alpha$ gene or to a segment of said gene.

55. (Previously presented) The targeting vector of claim 54, wherein said expression cassette is flanked by site-specific recombination sequences.

56. (Currently amended) The targeting vector of claim 55 wherein said sequences are LoxP sequences of Cre recombinase.

57. (Canceled)

58. (Currently Amended) The targeting vector of claim ~~57~~ 53, wherein said fragments of sequences consist of the sequences SEQ ID NO: 7 and SEQ ID NO: 8, corresponding respectively to positions 131281 to 136441 and 140101 to 145032 in the sequence of murine chromosome 12 (accession number AC073553 in the EMBL/GenBank database).

59. (Currently Amended) ~~An~~ A mouse embryonic cell ~~of a nonhuman mammal, which is~~
modified with the targeting vector of claim 53.

60-73 (Withdrawn)